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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,142	03/31/2000	JEAN MARTINEZ	427.034	1834
7590 10/09/2003 CHARLES A MUSERLIAN BIERMAN MUSERLIAN AND LUCAS 600 THIRD AVENUE NEW YORK, NY 10016			EXAMINER SAKELARIS, SALLY A	
			ART UNIT 1634	PAPER NUMBER

DATE MAILED: 10/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/486,142	MARTINEZ ET AL.	
	Examiner	Art Unit	
	Sally A Sakelaris	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 July 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 26-29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 26-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This action is written in response to applicant's correspondence submitted 7/08/2003. Claims 26-29 have been amended, claims 1-25 and 30-32 have been canceled, and no new claims have been added. Claims 26-29 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 26, 27, 28, and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With respect to claim 26, claim 26 is drawn broadly to single stranded oligonucleotides having 9 to 42 nucleotides of the sequence Y1-Y2-Y3-Y4-Y5(Y6-Y7-Y8-Y9) wherein among other things, Y1 and Y9 are nucleotide sequences of 1 to 12 nucleotides or are absent and Y7 is a trinucleotide which codes for any amino acid. A review of the full content of the specification indicates that the nucleotides of the sequence, Y1-Y2-Y3-Y4-Y5(Y6-Y7-Y8-Y9), are essential to the operation and function of the claimed invention.

With respect to claim 29, claim 29 is drawn broadly to a single-stranded oligonucleotide OZ having 15 to 39 nucleotides and capable of hybridizing under mild or stringent conditions with a consensus signal characteristic of amidated polypeptide hormones with the sequence having the formula Z1-Z2-Z3-Z4-Z5-Z6-Z7 wherein, among other things, Z1 and Z7 are nucleotide sequences of 1 to 12 nucleotides or are absent, and Z4 and Z5 are two trinucleotides which code for any two amino acids. The specification indicates that the nucleotides of the sequence, Z1-Z2-Z3-Z4-Z5-Z6-Z7, are essential to the operation and function of the claimed invention. A review of the language of the claims indicates that the claims are drawn to a genus, i.e., any nucleic acid that minimally contains these aforementioned sequences in addition to any full length gene which contains the sequence, any splice variants, or cDNAs. The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed”. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the

claimed genus. At section B(1), the court states that “An adequate written description of a DNA...’ requires a precise definition, such as by structure, formula, chemical name, or physical properties’, not a mere wish or plan for obtaining the claimed chemical invention”. In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. The present claims encompass full-length genes, cDNAs and other oligonucleotides whose exact composition that are not further described. There is substantial variability among the species of DNAs encompassed within the scope of claims 26-29 because an oligonucleotide having 9 to 42(Claim 26) or 15-39(Claim 29) nucleotides of their respective “OY” and “OZ” sequences, wherein some positions can be any amino acid and in still others, the nucleotides need only to hybridize under mild conditions with a consensus signal with the sequence, Z1-Z2-Z3-Z4-Z5-Z6-Z7, encompass a great deal more than just the enumerated sequences listed. The specification describes sequences OY and OZ as oligos which hybridize with a DNA sample and identifies a sequence in the sample, of at least one non-amidified precursor of peptides with an optional amidated C-terminal end position. Further, the specification provides only that this claimed “hybridization” takes place if two oligonucleotides have substantially complementary nucleotide sequences, and that they can combine over their length by establishing bonds(Pg.6). The specification does not limit the amount of sequences capable of hybridizing, by including an amount of similarity across a certain length that is necessary for hybridizing. Also, the specification states that certain OY or OZ nucleotides can encode a wide variety of amino acids with differing lengths, not to mention that certain amino acids may or may not even be present. Furthermore, the specification does not teach all of the possible structures that could exist for the

OY and OZ oligonucleotides. The specification also does not teach how the very different possible structures claimed, share similar functions. The claims are written such that they encompass sequences of any length and composition for certain amino acid positions which only minimally contain the few, requisite trinucleotide sequences and amino acids as specified in claims 26 and 29, but, could include genes and/or regulatory domains which have not been described and of which applicant does not appear to have been in possession.

Weighing all factors, 1) partial structure of the DNAs of an oligonucleotide having 9 to 42(Claim 26) or 15-39(Claim 29) nucleotides of their respective “OY” and “OZ” sequences, wherein some positions can be any amino acid and in still others, the nucleotides need only to “hybridize” under mild conditions with a consensus signal with the sequence, Z1-Z2-Z3-Z4-Z5-Z6-Z7, encompass a great deal more than just the enumerated sequences listed, 2) the breadth of the claim as reading on genes yet to be discovered in addition to numerous splice variants and cDNAs, 3) the lack of correlation between the structure and the function of the genes and/or splice variants; in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the genus of oligonucleotides having 9 to 42(Claim 26) or 15-39(Claim 29) nucleotides of their respective “OY” and “OZ” sequences, wherein some positions can be any amino acid and in still others, the nucleotides need only to “hybridize”(in the very broadly defined manner of the specification) under mild conditions with a consensus signal with the sequence, Z1-Z2-Z3-Z4-Z5-Z6-Z7.

Response to Arguments:

Applicant correctly asserted that “comprising” is open language. Applicant should also note that “having” is open language and has the same scope as “comprising”. If applicant intends to achieve closed language, they could use “consisting of”.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 26-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 27 and 29 are indefinite over the recitation of “suppressed.” It is not clear if the applicant intended to mean that the “suppressed” sequence was absent from the oligos or if the sequence was just not expressed from the oligos. Applicant should amend the claims to make definite their intentions for a “suppressed” oligo.

Response to Arguments:

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term “suppressed” in claims 26, 27, and 29 is used by the claim to mean “absent”, while the accepted meaning is “to inhibit the genetic expression of (Merriam Webster),” “Checking of abnormal flow or discharge”(Stedman’s Medical Dictionary), or as a Molecular biology book defines

suppressor genes in that they “do not act by changing the nucleotide sequence of a mutant gene. Instead they change the way the mRNA template is read” (Watson et al. Pg. 446). The art does not use the term to mean absent. The term is indefinite because the specification does not clearly redefine the term.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

3. Claims 26, 27, and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Croce et al. (US 6,040,140).

Croce et al. teach SEQ ID NO:1, a single stranded oligonucleotide OY having 9 to 42 nucleotides of the sequence Y1-Y2-Y3-Y4-Y5 wherein Y1 is absent, Y2 is a trinucleotide which

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encodes for Gly, Y3 is a nucleotide coding for Arg and Y5 is a nucleotide sequence, Y6-Y7-Y8-Y9 wherein Y6 is a trinucleotide which codes for Ser, Y7 is a trinucleotide which codes for Ala, Y8 is a trinucleotide which codes for Glu and Y9 is absent. Please see attached alignment of OY and SEQ ID NO:1.

Response to Arguments:

Applicant asserts that since “comprising” was replaced by “having”, they have obviated the rejection. While the examiner acknowledges the argument, she points applicant to the above written description rejection where it is explained that both terms represent open language and as a result the art still anticipates the claims.

4. Claim 29 is rejected under 35 U.S.C. 102(b) as being anticipated by Draper (US 5,610,054).

Draper teaches SEQ ID NO: 279, a single-stranded oligonucleotide OZ having 15 to 39 nucleotides and hybridizes under mild or stringent conditions with a consensus signal characteristic of amidated polypeptide hormones with the sequence having the formula Z1-Z2-Z3-Z4-Z5-Z6-Z7 wherein Z1 is absent, Z2 and Z3 are two trinucleotides which code for Leu, Z4 and Z5 are two trinucleotides which code for any two amino acids, Z6 is a trinucleotide which codes for Leu and Z7 is a nucleotide sequence that is absent. Please see attached alignment of OZ and SEQ ID NO: 279. Draper further teaches “a group of oligonucleotides”(being interpreted as multiple copies of same OZ) OZ's, as these target mRNA sequences are harvested from the HCV genomic RNA, containing additional copies of OZ, not just a single OZ is present(Col. 4).

Response to Arguments:

Applicant asserts that since “comprising” was replaced by “having”, they have obviated the rejection. While the examiner acknowledges the argument, she points applicant to the above written description rejection where it is explained that both terms represent open language and as a result the art still anticipates the claims. Furthermore, applicant asserts that since the “aim of Draper is really different from Applicants’ invention”(Pg. 6). Applicant is reminded that limitations in the specification cannot be read into the claims and be given patentable weight.

***THE FOLLOWING GROUNDS OF REJECTION HAVE BEEN NECESSITATED
BY APPLICANTS AMENDMENTS***

Claims 26-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes “If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).”

In the instantly rejected claims, the new limitation of “suppressed with the exception of CGACACUCCACCAUA.” in claim 26 appears to represent new matter. No specific basis for this limitation was identified in applicant’s paper, nor did a review of the specification by the examiner find any basis for the limitation. Specifically, the exclusion proviso in which "all others" are distinguished is not found in the specification. As noted by MPEP 2173.05(i),

“Any negative limitation or exclusionary proviso must have basis in the original disclosure. See *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983) *aff'd mem.*, 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement.”

Since no basis has been identified, the claims are rejected as incorporating new matter.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communication from the examiner should be directed to Sally Sakelaris whose telephone number is (703) 306-0284. The examiner can normally be reached on Monday-Thursday from 7:30AM-5:00PM and Friday from 1:00PM-5:00PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W.Gary Jones, can be reached on (703)308-1152. The fax number for the Technology Center is (703)305-3014 or (703)305-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to Chantae Dessau whose telephone number is (703)605-1237.

Sally Sakelaris



October 8, 2003



JEFFREY FREDMAN
PRIMARY EXAMINER